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(54) **Oral and /or topical compositions**

(57) Suggested are new advantageous oral and/or topical compositions, comprising

(a) prebiotics and

(b) extracts of hoodia and/or their active steroid glycosides.

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Description**Field of the invention**

5 **[0001]** The present invention is related to the area of alimentation and concerns oral and/or topical compositions comprising certain plant extracts and prebiotics, dietary supplements and food compositions comprising said plant extracts and prebiotics, and the use of mixtures comprising said plant extracts and prebiotics for improving the stimulation of the growth of healthy bacteria.

Background of the invention

10 **[0002]** Probiotics contain live bacteria and represent an important part of the complex world of foods that are good for health. It's the bacteria and the metabolites which they produce that give these products their health promoting properties. The best known example of a probiotic is yoghurt. The experimental data for yoghurt is still not as conclusive as one would like, however, human studies related to the consumption of dietary milk products show increased milk digestibility, quicker recovery from certain types of diarrhoea, enhanced immune function, relation in certain cancers, and possible lowering of blood cholesterol levels.

15 **[0003]** Bacteria found in products like yoghurt, kefir or fermented vegetables usually aren't found in the human intestine. In fact, the intestinal environment is often a hostile one for these foreign bacteria. Because of this, bacteria eaten in probiotic products don't colonise the intestine but are flushed through and eliminated from the body.

20 **[0004]** The bacteria living in the intestine make up a very large and very diverse population. The numbers of each kind of bacteria change depending on age, diet, health status, and use of drugs and supplements. The effects are linked to the ability of the bacteria to adhere to the intestinal wall and use the semi-digested food that it passing through the intestines. It is not surprising to found that the bacterial population in the intestines of vegetarians is much different compared to that of meat eaters. Because some bacteria have specific nutrient requirements it has been proposed that adding these particular foods or nutrients to the diet could be a way of increasing the numbers of specific bacteria. Such additives are called "prebiotics". Thus, to be effective, prebiotics must escape digestion in the upper gastrointestinal tract and be used by a limited number of the micro-organisms comprising the colonic microflora. Typical examples for well-known prebiotics are oligosaccharides, e.g. in 1995 Gibson et al. found that oligofructose and inulin, when fed to humans, selectively stimulated the growth of bifidobacteria without influencing the numbers of lactobacillus. Since prebiotics mainly stimulate the growth of bifidobacteria, for which reason the also are referred to as bifidogenetic factors.

25 **[0005]** Although various types of prebiotics are known from the literature and can be found in the market there is still an increasing need for more active alternatives or additives which support the various activities of existing products in synergistic manner. Therefore, the object of the present invention has been to provide a new system of prebiotic compounds which shows a synergistic stimulation of the growth of healthy bacteria, preferably bifido and lactic bacteria both.

Detailed description of the invention

30 **[0006]** The present invention refers to oral and/or topical compositions, comprising

- 40 (a) prebiotics and
(b) extracts of hoodia and/or their active steroid glycosides.

45 **[0007]** Surprisingly it has been observed that mixtures of said extracts of hoodia and more particular the active steroid glycosides obtainable from said extracts on one hand and prebiotics on the other show a synergistic behaviour with respect to stimulation of growth of bacteria selected from the group consisting of *Bifidobacterium breve*, *Bifidobacterium infantis*, *Bifidobacterium longum* and *Bifidobacterium adolescentis* on one hand, and *Lactobacillus bulgaricus*, *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus plantarum*, *Streptococcus faecium*, and *Streptococcus thermophilus* on the other.

Prebiotics

50 **[0008]** Prebiotics are defined as non-digestible food ingredients that may beneficially affect the host be selectively stimulating the growth and/or the activity of a limited number of bacteria in the colon. The following describes the various oligosaccharides which can be taken into account as suitable prebiotics (component a):

• Fructooligosaccharides

5 [0009] Fructooligosaccharides or FOS typically refers to short-chain oligosaccharides comprised of D-fructose and D-glucose, containing from three to five monosaccharide units. FOS, also called neosugar and short-chain FOS, are produced on a commercial scale from sucrose using a fungal fructosyltransferase enzyme. FOS is resistant to digestion in the upper gastrointestinal tract. They act to stimulate the growth of *Bifidobacterium* species in the large intestine. FOS is marketed in the United States in combination with probiotic bacteria and in some functional food products.

10 • Inulins

15 [0010] Inulins refer to a group of naturally-occurring fructose-containing oligosaccharides. Inulins belong to a class of carbohydrates known as fructans. They are derived from the roots of chicory (*Cichorium intybus*) and Jerusalem artichokes. Inulins are mainly comprised of fructose units and typically have a terminal glucose. The bond between fructose units in inulins is a beta-(2-1) glycosidic linkage. The average degree of polymerisation of inulins marketed as nutritional supplements is 10 to 12. Inulins stimulate the growth of *Bifidobacterium* species in the large intestine.

• Isomaltooligosaccharides

20 [0011] Isomaltooligosaccharides comprise a mixture of alpha-D-linked glucose oligomers, including isomaltose, panose, isomaltotetraose, isomaltopentaose, nigerose, kojibiose, isopanose and higher branched oligosaccharides. Isomaltooligosaccharides are produced by various enzymatic processes. They act to stimulate the growth of *Bifidobacterium* species and *Lactobacillus* species in the large intestine. Isomalto oligosaccharides are marketed in Japan as dietary supplements and in functional foods. They are being developed in the United States for similar uses.

25 • Lactilol

30 [0012] Lactilol is a disaccharide analogue of lactulose. Its pharmaceutical use is in the treatment of constipation and hepatic encephalopathy. Lactilol is also used in Japan as a prebiotic. It is resistant to digestion in the upper gastrointestinal tract and it is fermented by a limited number of colonic bacteria, resulting in an increase in the biomass of bifidobacteria and lactobacilli in the colon. Lactilol is known chemically as 4-O-(beta-D-galactopyranosyl)-D-glucitol. Lactilol is not approved for the treatment of hepatic encephalopathy or constipation in the U.S., and its use as a prebiotic is considered experimental. Lactilol is used in Europe as a food sweetener.

35 • Lactosucrose

40 [0013] Lactosucrose is a trisaccharide comprised of D-galactose, D-glucose and D-fructose. Lactosucrose is produced enzymatically by the enzymatic transfer of the galactosyl residue in lactose to sucrose. Lactosucrose is resistant to digestion in the stomach and small intestine. It is selectively utilized by intestinal *Bifidobacterium* species resulting in significant induction of growth of these bacteria in the colon. Therefore, under physiological conditions, lactosucrose acts on the intestinal microflora as a growth factor for *Bifidobacterium* species. Lactosucrose is also known as 4G-beta-D-galactosylsucrose. It is widely used in Japan as a dietary supplement and in functional foods, including yoghurt. Lactosucrose is being developed in the United States for similar uses.

45 • Lactulose

50 [0014] Lactulose is a semi-synthetic disaccharide comprised of the sugars D-lactose and D-fructose. The sugars are joined by a beta-glycosidic linkage, making it resistant to hydrolysis by human digestive enzymes. Lactulose is, however, fermented by a limited number of colonic bacteria. This can lead to changes in the colonic ecosystem in favour of bacteria, such as lactobacilli and bifidobacteria, which may confer some health benefits. Lactulose is a prescription drug in the United States for the treatment of constipation and hepatic encephalopathy. It is marketed in Japan for use as a dietary supplement and in functional foods. Its use in the United States as a prebiotic substance is still experimental. • Pyrodextrins

55 [0015] Pyrodextrins comprise a mixture of glucose-containing oligosaccharides that is derived from the hydrolysis of starch. Pyrodextrins have been found to promote the proliferation of *Bifidobacterium* species in the large intestine. They are resistant to digestion in the upper gastrointestinal tract. Pyrodextrins are being developed for the nutritional supplement market place.

• Soy oligosaccharides

[0016] Soy oligosaccharides refer to oligosaccharides found in soybeans and also in other beans and peas. The two principal soy oligosaccharides are the trisaccharide raffinose and the tetrasaccharide stachyose. Raffinose comprises one molecule each of D-galactose, D-glucose and D-fructose. Stachyose consists of two molecules of D-galactose, one molecule of D-glucose and one molecule of D-fructose. Soy oligosaccharides act to stimulate the growth of *Bifidobacterium* species in the large intestine. They are marketed in Japan as dietary supplements and in functional foods. They are being developed in the United States for similar uses.

• Transgalactooligosaccharides

[0017] Transgalactooligosaccharides (TOS) are a mixture of oligosaccharides consisting of D-glucose and D-galactose. TOS are produced from D-lactose via the action of the enzyme beta-galactosidase obtained from *Aspergillus oryzae*. TOS are resistant to digestion in the upper gastrointestinal tract and stimulate the growth of bifidobacteria in the large intestine. TOS are marketed in Japan and Europe as dietary supplements and are used in functional foods. They are being developed for similar use in the United States.

• Xylooligosaccharides

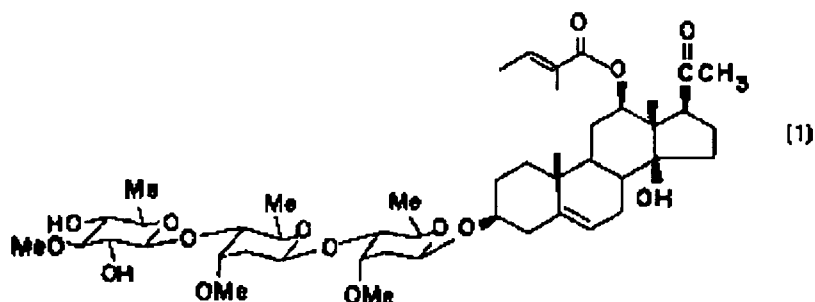
[0018] Xylooligosaccharides are comprised of oligosaccharides containing beta (1→4) linked xylose residues. The degree of polymerisation of xylooligosaccharides is from two to four. Xylooligosaccharides are obtained by enzymatic hydrolysis of the polysaccharide xylan. They are marketed in Japan as prebiotics and are being developed for similar use in the United States.

• Beta Glucans

[0019] Suitable beta-glucans include those originating from plants including cereals such as oats and barley, fungi, yeast, and bacteria. In addition, microbial cell wall preparations and whole cells rich in beta glucans are also suitable sources for beta glucan preparations useful for the present invention. Monomer residues in glucans can have 1-3 and 1-4, or 1-3 and 1-6 linkages (that is the monomer units are joined through 1,3, 1,4 or 1,6 bonds) and the percent of each type can vary. Preferably, beta glucans derived from yeast, particularly from *Saccharomyces*, preferably *Saccharomyces cerevisiae*, are used for the present invention. It will be appreciated, however, that other beta glucans would also be suitable.

Extracts of Hoodia

[0020] *Hoodia* is a South African cactus plant that was traditionally used by the original population during hunting periods to suppress appetite. It has been found that this special property is linked to its content of active steroid glycosides. In 2001/2002 one of these actives, called Substance P57,



was identified and isolated. Since weight management in general and the reduction of appetite in particular have become an important health claim with increasing economic impact for all producers of so-called functional food or dietary supplements, it has been found desirable to develop an extract of *Hoodia* with a high content of its active principles which can be used for weight control and prevention of obesity.

[0021] International patent application WO 98/046243 A1 (CSIR) discloses a pharmaceutical composition based on

an extract obtainable from a plant of the genus *Trichocaulon* or *Hoodia* containing an appetite suppressant agent. Also provided is a manufacturing process including the steps of treating collected plant material with a solvent to extract a fraction having appetite suppressant activity, separating the extraction solution from the rest of the plant material, removing the solvent from the extraction solution and recovering the extract.

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Oral and/or topical compositions

[0022] The oral and/or topical compositions according to the present invention may comprise the prebiotics and the extracts of hoodia or their active steroid glycosides in a weight ratio of 99:1 to 50:50 and more particularly 95:10 to 75:25. The highest synergistic effects, however, are observed at ratios of 92:8 to 80:20. In general, the compositions can be used in a concentration of up to about 10, particularly 0.5 to 8 and more particularly 1 to 2 % b.w. - calculated on the probiotic micro-organisms being present in the final food composition. One percent, however, has been found to be particularly suitable.

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[0023] In a special embodiment of the present invention said compositions are macro- or micro-encapsulated. "Microcapsules" are understood to be spherical aggregates with a diameter of about 0.1 to about 5 mm which contain at least one solid or liquid core surrounded by at least one continuous membrane. More precisely, they are finely dispersed liquid or solid phases coated with film-forming polymers, in the production of which the polymers are deposited onto the material to be encapsulated after emulsification and coacervation or interfacial polymerization. In another process, liquid active principles are absorbed in a matrix ("micro-sponge") and, as microparticles, may be additionally coated with film-forming polymers. The microscopically small capsules, also known as nanocapsules, can be dried in the same way as powders. Besides single-core microcapsules, there are also multiple-core aggregates, also known as microspheres, which contain two or more cores distributed in the continuous membrane material. In addition, single-core or multiple-core microcapsules may be surrounded by an additional second, third etc. membrane. The membrane may consist of natural, semisynthetic or synthetic materials. Natural membrane materials are, for example, gum arabic, agar agar, agarose, maltodextrins, alginic acid and salts thereof, for example sodium or calcium alginate, fats and fatty acids, cetyl alcohol, collagen, chitosan, lecithins, gelatin, albumin, shellac, polysaccharides, such as starch or dextran, polypeptides, protein hydrolyzates, sucrose and waxes. Semisynthetic membrane materials are inter alia chemically modified celluloses, more particularly cellulose esters and ethers, for example cellulose acetate, ethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose and carboxymethyl cellulose, and starch derivatives, more particularly starch ethers and esters. Synthetic membrane materials are, for example, polymers, such as polyacrylates, polyamides, polyvinyl alcohol or polyvinyl pyrrolidone. Examples of known microcapsules are the following commercial products (the membrane material is shown in brackets) *Hallcrest Microcapsules* (gelatin, gum arabic), *Coletica Thalaspheeres* (maritime collagen), *Lipotec Millicapseln* (alginic acid, agar agar), *Induchem Unispheres* (lactose, microcrystalline cellulose, hydroxypropylmethyl cellulose), *Unicerin C30* (lactose, microcrystalline cellulose, hydroxypropylmethyl cellulose), *Kobo Glycospheres* (modified starch, fatty acid esters, phospholipids), *Softspheres* (modified agar agar), *Kuhs Probiol Nanospheres* (phospholipids) and *Primaspheres* or *Primasponges* (chitosan, anionic polymers).

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Food compositions

[0024] A further object of the present invention relates to food compositions, comprising

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- (a) prebiotics and
- (b) extracts of hoodia or their active steroid glycosides.

[0025] The compositions may further comprise certain plant extracts, like extracts of *Camellia sinensis* (Green tea) or *Olea europensis* (Olive tree) which are rich in actives like polyphenols, oleuropein and hydroxytyrosol.

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Industrial application

[0026] A final object of the present invention is related to the use of mixtures, comprising

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- (a) prebiotics and
- (b) extracts of hoodia or their active steroid glycosides

for stimulating the growth of healthy bacteria, for example in the stomach (if applied oral) or on skin (if administered topical).

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Examples

Examples 1 to 10, Comparative Examples C1 to C 10

5 **[0027]** The stimulation of growth of micro-organisms has been studied by enumerating *bifidobacterium* and *lactobacilli* in vitro in the presence of various test substances. More specifically, aliquots (1 mL) of human faecal homogenates (10 g per 100 mL diluent) were added to diluted WC broth (diluted 50:50 with 0.05M phosphate buffer) to which were added the test mixtures and a lactobacillus or bifidobacterium strain. For each of the combinations, parallel tubes were prepared with one set being inoculated with *Bifidobacterium spp* or *Lactobacillus spp*. All mixtures were then incubated for up to 10 24 hours and bacterial numbers enumerated. The results are presented in Tables 1 and 2:

Table 1 Effect of 1 % prebiotic, hoodia and prebiotic/hoodia mixture on *Bifidobacterium*

	0	C1	C2	C3	C4	C5	1	2	3	4	5
15 Inulin	-	1.0	-	-	-	-	0.8	0.9	-	-	-
Lactosucrose	-	-	1.0	-	-	-	-	-	0.9	-	-
Lactolin	-	-	-	1.0	-	-	-	-	-	0.9	-
20 Betaglucan	-	-	-	-	1.0	-	-	-	-	-	0.9
Hoodia Extr.	-	-	-	-	-	1.0	0.2	-	-	-	-
Hoodia Extr.	-	-	-	-	-	-	-	0.1	0.1	-	-
Hoodia Extr.	-	-	-	-	-	-	-	-	-	0.1	-
25 Hoodia Extr.	-	-	-	-	-	-	-	-	-	--	0.1
Bacterial numbers (CFU/ml)	1.0 x 10 ⁶	1.5 x 10 ⁷	1.1 x 10 ⁷	1.6 x 10 ⁷	1.2 x 10 ⁷	1.0 x 10 ⁶	3.1 x 10 ⁷	3.0 x 10 ⁷	3.1 x 10 ⁷	2.9 x 10 ⁷	2.4 x 10 ⁷
30 Hoodia Extr.:	Spraydried extract prepared according to WO 98/046243 A1										

35 **[0028]** Starting from a control of 1.0 10⁶ CFU/ml (0) the addition of 1 % b.w. of various prebiotics (Comparative Examples C1-C4) increases the CFU by a factor of 10, while the addition of the hoodia extract alone does only have a weak effect on the stimulation of cell growth (Comparative Examples C5). Adding however mixture of prebiotics and hoodia extract to the samples, the CFU numbers were multiplied by a factor of about 40 (Inventive Examples 1 to 5). The highest synergistic effect can be seen at a relation prebiotic:hoodia of about 90 : 10.

Table 2 Effect of 1 % prebiotic, hoodia and prebiotic/hoodia mixture on *Lactobacterium*

	0	C6	C7	C8	C9	C10	6	7	8	9	10
40 Inulin	-	1.0	-	-	-	-	0.8	0.9	-	-	-
Lactosucrose	-	-	1.0	-	-	-	-	-	0.9	-	-
Lactolin	-	-	-	1.0	-	-	-	-	-	0.9	-
45 Betaglucan	-	-	-	-	1.0	-	-	-	-	-	0.9
Hoodia Extr.	-	-	-	-	-	1.0	0.2	-	-	-	-
Hoodia Extr.	-	-	-	-	-	-	-	0.1	0.1	-	-
Hoodia Extr.	-	-	-	-	-	-	-	-	-	0.1	-
50 Hoodia Extr.	-	-	-	-	-	-	-	-	-	-	0.1
Bacterial numbers (CFU/ml)	2.8 x 10 ⁵	1.4 x 10 ⁶	1.1 x 10 ⁶	1.5 x 10 ⁶	1.1 x 10 ⁶	4.4 x 10 ⁵	6.1 x 10 ⁶	6.2 x 10 ⁶	6.2 x 10 ⁶	6.2 x 10 ⁶	6.7 x 10 ⁶
55 Hoodia Extr.:	Spraydried extract prepared according to WO 98/046243 A1										

[0029] Starting from a control of $2.8 \cdot 10^5$ CFU/ml (0) the addition of 1 % b.w. of various prebiotics (Comparative Examples C6-C9) increases the CFU by a factor of 4, while the addition of the hoodia extract alone does only have a weak effect on the stimulation of cell growth (Comparative Examples C10). Adding however, mixture of prebiotics and hoodia extracts to the samples, the CFU numbers were multiplied by a factor of about 15 (Inventive Examples 6 to 10). The highest synergistic effect can be seen again at a relation prebiotic:hoodia of about 90 : 10.

Example 11

Yoghurt composition

[0030] Soy milk is added to 15-75 parts by volume of cow milk to make 100 parts of the mixture. The mixture is then pasteurised at about 90 °C for 15 seconds and then cooled. The cooled, pasteurised mixtures are then inoculated with 3 to 5 percent by volume of a yoghurt culture having 1:1 ratio of *Lactobacillus bulgaricus* and *Bifidobacterium adolescentis*. The incubation is carried out at about 42 °C. In about 2 hours thickening will occur. The fermentation is carried out for about 5.5 hours. The yoghurt compositions thus obtained is treated with 1 % - calculated on the amount of micro-organisms being present - of a 9:1 mixture of inulin and spray-dried hoodia extract. The products firm consistency and have a flavour like or substantially indistinguishable from that of a corresponding yoghurt composition using 100 percent of fresh cow milk. A small amount of citric acid can be added to the fermentation mixture to enhance the flavour of the final yoghurt composition. A suitable amount of citric acid is 0.5 percent based on the weight of the composition.

Claims

1. Oral and/or topical compositions, comprising
 - (a) prebiotics and
 - (b) extracts of hoodia or their active steroid glycosides
2. Compositions according to claim 1, **characterised in that** said prebiotics (component a) are selected from the group consisting of fructooligosaccharides, inulins, isomaltooligosaccharides, lactilol, lactosucrose, Lactulose, Pyrodextrins, soy oligosaccharides, transgalactooligosaccharides, xylooligosaccharides and beta glucans.
3. Compositions according to claims 1 and/or 2, **characterised in that** said steroid glycosides are Substance P57 or their analogues, homologues or isomers.
4. Compositions according to any of the claims 1 to 3, **characterised in that** they comprise components (a) and (b) in weight ratios of from 99:1 to 50:50.
5. Compositions according to any of the claims 1 to 4, **characterised in that** said mixtures are used in amounts of up to 10 % b.w. calculated on the micro-organisms being present in the final food composition.
6. Compositions according to any of the claims 1 to 5, **characterised in that** said mixtures are macro- or micro-encapsulated.
7. Food compositions, comprising
 - (a) prebiotics and
 - (b) extracts of hoodia and/or their active steroid glycosides
8. Use of mixtures, comprising
 - (a) prebiotics and
 - (b) extracts of hoodia and/or their active steroid glycosides

for stimulating the growth of healthy bacteria.



European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention EP 06 01 8919 shall be considered, for the purposes of subsequent proceedings, as the European search report

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 2006/045112 A2 (SHATKINA LIMA [US]; SHATKINA RUFINA [US]; GUREVICH SAM [US]) 27 April 2006 (2006-04-27) * claims 1,2,7-9,21 * * page 5, paragraphs 14,15 * * page 7, paragraph 19 * * page 8, paragraph 22 * -----	1-7	INV. A23L1/30 A23L1/308 A61K36/27 A61P1/00 A23C9/13
X	WO 2006/079056 A (HOLT STEPHEN [US]) 27 July 2006 (2006-07-27) * claims 1,21; example 2 * * page 2, line 23 - page 3, line 10 * * page 11, lines 6,7 * -----	1-7	
X	WO 2005/039493 A2 (TRIMSPA CORP [US]; FLEISCHNER ALBERT M [US]) 6 May 2005 (2005-05-06) * claims 1,7,11 * * page 7, line 17 - page 8, line 13 * -----	1,3-5,7,8	
X	US 2005/276839 A1 (RIFKIN CALMAN H [US]) 15 December 2005 (2005-12-15) * claims 1,45; examples 1,2,7 * ----- -/--	1,3-5,7,8	TECHNICAL FIELDS SEARCHED (IPC) A23L A61K
INCOMPLETE SEARCH			
<p>The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.</p> <p>Claims searched completely :</p> <p>Claims searched incompletely :</p> <p>Claims not searched :</p> <p>Reason for the limitation of the search: see sheet C</p>			
Place of search The Hague		Date of completion of the search 6 March 2007	Examiner Tallgren, Antti
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p>		<p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>	

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EPO FORM 1503 03.82 (P04C07)



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	AU 2006 100 120 A4 (BIOVITAL PTY LTD) 6 April 2006 (2006-04-06) * page 2, line 17 - page 4, line 7; claims 1,2 *	1,3-5,7	
A	----- EP 1 600 061 A (COGNIS IP MAN GMBH [DE]) 30 November 2005 (2005-11-30) * claims 1,8,10; examples 1-11 * -----	1-8	
			TECHNICAL FIELDS SEARCHED (IPC)



Claim(s) searched completely:
1-4,6-8

Claim(s) searched incompletely:
5 (partially)

Reason for the limitation of the search:

Claim 5 does not meet the requirements of Article 84 EPC in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved (10 % of the micro-organism present). Such a definition is only allowable under the conditions elaborated in the Guidelines C-III, 4.7. In this instance, however, such a formulation is not allowable because it appears possible to define the subject-matter in more concrete terms, viz. in terms of how the effect is to be achieved (amount of ingredients in composition).

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 06 01 8919

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
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06-03-2007

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REFERENCES CITED IN THE DESCRIPTION

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